

RESEARCH REPORT

Substance misuse and psychiatric illness: prospective observational study using the general practice research database

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Objectives: To quantify the relation between substance misuse and psychiatric illness in the UK general practice population in terms of (a) the relative risk of developing one condition given prior exposure to the other and (b) the proportion of cases of one condition attributable to exposure to the other.

Design: Population based prospective observational study using the general practice research database (GPRD) between 1993 and 1998. The 230 GP practices represent 3.1% of the population.

Setting: England and Wales.

Participants: 1.4 million registered patients of whom 3969 had both substance misuse and psychiatric diagnoses between 1993 and 1998.

Main outcome measures: Relative risk (RR) for subsequent psychiatric illness among participants exposed to substance misuse and RR for subsequent substance misuse among participants exposed to psychiatric illness. Population attributable risk (PAR) of psychiatric illness attributable to substance misuse and of substance misuse attributable to psychiatric illness.

Results: The baseline prevalence of psychiatric illness over the study period was 15% and 0.3% for substance abuse. RR for psychiatric illness for substance misusers compared with non-substance misusers was 1.54 (95% CI 1.47 to 1.62). RR for substance misuse among psychiatric compared with non-psychiatric cases was 2.09 (95% CI 1.99 to 2.22). PAR for psychiatric illness attributable to substance misuse was 0.2%. PAR for substance misuse attributable to psychiatric illness was 14.2%.

Discussion: Only a comparatively small proportion of psychiatric illness seems possibly attributable to substance use whereas a more substantial proportion of substance use seems possibly attributable to psychiatric illness. This study does not support the hypotheses that comorbidity between substance misuse and psychiatric illness is primarily the result of substance misuse or that increasing comorbidity is largely attributable to increasing substance misuse.

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Comorbidity of problematic use of illicit drugs ("substance misuse") and psychiatric illness is increasing among people presenting in UK primary care settings.¹ Several cross sectional studies have reported that users of opioids, stimulants, and cannabis have higher prevalence rates of psychiatric illness compared with non-users.^{2,3} The temporal relation between drug use and psychiatric illness is important because prior drug use may be a causal factor for the psychiatric illness and vice versa. This is a complex topic to investigate for several reasons. Firstly, it requires longitudinal data to ascertain causal sequences. Secondly, rates of substance misuse and psychiatric illness in general population studies tend to be low and thus power may be limited. Thirdly, it is necessary to consider potentially confounding factors and most extant studies are limited in their ability to do this.⁴ A 1990 review of the evidence on cannabis and functional psychoses cautiously concluded that "when examined critically... there is some weak evidence that long term or heavy users of cannabis may occasionally develop acute psychoses".⁵ More recently there have been stronger claims. A Dutch prospective population study showed that "the maximum proportion of psychosis outcomes attributable to cannabis use in psychosis-free subjects—is higher than 50 percent."⁶ In contrast, a study of people selected on the basis of their being at very high risk for the onset of psychoses concluded that "neither cannabis use nor dependence in the year prior to recruitment...contributed to the risk of developing psychosis".⁷ Also, increasing cannabis use

in the general population does not seem to be associated with an increased incidence of schizophrenia.⁸ It is therefore, currently, difficult to draw any secure conclusions on the contribution of cannabis use to the population burden of mental illness and even more difficult (as evidence is even more sparse) to make such inference with regard to other, illicit, substances of misuse.

More generally, increasing population rates of substance misuse may underlie increasing comorbidity without there being a causal relation between the two, simply because more people with mental illness have access to drugs. Secondly, substance misuse and psychiatric illness may share common antecedents. Increases in these risk factors may have led independently to increases in both conditions.

This study uses clinical diagnoses of substance misuse and psychiatric illness among 1.8 million people represented in the UK general practice research database (GPRD). These people attended UK general practitioners between 1993 and 1998 and at study entry point they had not received a clinical diagnosis of either substance misuse and psychiatric illness. The latter point is important because establishing causality is less likely to be problematic among people who have not been diagnosed with either type of condition.⁹ By examining the temporal sequence of diagnosis in this cohort we were able to explore two hypotheses. Firstly, that prior substance misuse is associated with an increased risk of developing psychiatric illness; secondly, that prior psychiatric illness is associated with an increased risk of substance misuse. We also

Table 1 Relative risk of psychiatric illness and substance misuse

% Non-substance misusers who develop psychiatric illness 1993–1998	15.09
% Substance misusers who develop psychiatric illness 1993–1998	23.30
Relative risk of psychiatric illness (substance v non-substance abusers)	1.54
% Non-psychiatric cases who develop substance illness 1993–1998	0.37
% Psychiatric cases who develop substance misuse 1993–1998	0.77
Relative risk of substance misuse (psychiatric v non-psychiatric cases)	2.09

estimated the proportion of cases of each condition attributable to exposure to the other assuming a causal relation between the two.

METHODS

The sampling frame for this study is the GPRD. The GPRD is the world's largest computerised database of patient records and is owned by the Medicines and Healthcare Products Regulatory Agency. Contributing GPs record all prescriptions and all significant morbidity and these data are subjected to routine quality assessment. The Office of National Statistics (ONS) supplied the data for this study. The data supplied included medical histories for all cases with a diagnosis of substance misuse and all cases meeting the definition of comorbidity described below. For all other patients, ONS supplied denominator data in the form of tables of patient years of exposure. Over the six year study period there were 6 202 083 patient years of exposure; of these 936 123 involved patients consulting for a psychiatric condition (15.1%) and 22 904 (0.37%) involved patients consulting for substance misuse.

Defining substance misuse disorders and psychiatric illness

As well as routine validation, GPRD psychiatric data have been the subject of an in depth study,¹⁰ which concluded that the accuracy of the computer categories for schizophrenia, non-affective psychosis, and all non-organic psychoses was good (88%–91%) and compared favourably with psychiatric case registers. As part of this study, we addressed concerns that substance misuse and psychiatric illness might not be recorded in GP records. Examination of over 200 sets of case notes showed that over 90% of patients treated for substance misuse or psychiatric illness in secondary care settings are known to their GP.¹¹

In this study, 1693 diagnostic codes for psychiatric illness were identified. These codes were classified into six diagnostic groups: (a) psychoses, (b) schizophrenia, (c) paranoia, (d) neurosis, (e) personality disorders, and (e) other disorders (which includes "insomnia not otherwise

specified", "behaviour problems", "hallucinations", "hallucinations auditory", "behaviour antisocial", and "disorder behaviour").

Altogether 258 Oxmis and Read codes for substance misuse disorders were identified. The main codes used (in descending order) were "drug addiction", "heroin addiction", "drug dependence", "drug abuse", "habitual drug abuse", "opiate abuse", "misuse of drugs", and "drug misuse". As in our previous paper,¹ all these diagnoses were defined as "substance misuse" for the purposes of this analysis. Because of low numbers, issues relating to specific substances are not addressed in this paper. This classification does not include alcohol or tobacco related disorders.

Comorbidity case definition

All patients were free from either substance misuse or psychiatric diagnosis for at least one year at study entry date. A case was defined as comorbid when a patient has received diagnoses for both psychiatric illness and substance misuse at some time between 1993 and 1998. Between 1993 and 1998 there were 3969 remaining comorbid cases, divided into three groups. Group 1: baseline substance misuse (substance misuse is first diagnosis in the study period); $n = 1588$. Group 2: baseline psychiatric illness (psychiatric illness is first diagnosis in the study period); $n = 2162$. Group 3: baseline comorbidity (that is, where both psychiatric illness and substance misuse are diagnosed on same day in the study period); $n = 219$.

Analysis

The relative risk of psychiatric illness among substance misusers compared with non-substance misusers was calculated as was the relative risk of substance misuse among psychiatric cases compared with non-psychiatric cases. The 95% confidence intervals for the relative risks were calculated.¹² Linear regression was performed to assess whether the proportion of comorbid cases with a baseline diagnosis of substance misuse changed significantly over the study period. The analysis was conducted using StatsDirect version 2.3.7 (<http://www.statsdirect.com>).

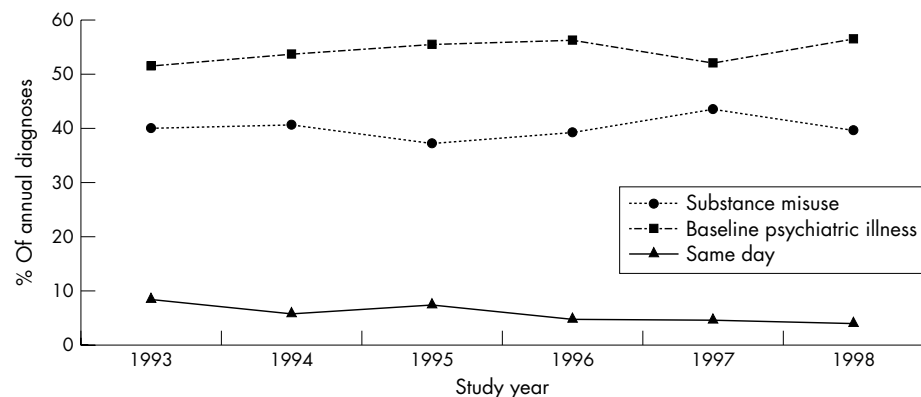


Figure 1 Annual proportions of first diagnoses among comorbid cases diagnosed each year from 1993 to 1998.

Table 2 Population attributable risk proportion of illness in the population attributable potentially explained by the exposure

Exposure	Illness	Population attributable risk (% of cases)	95% CI
Substance misuse	psychiatric illness (all)	0.2	0.17 to 0.22
Substance misuse	schizophrenia and psychoses	0.11	0.01 to 0.21
Psychiatric illness (all)	substance misuse	14.2	13.0 to 15.3
Schizophrenia and psychoses	substance misuse	0.76	0.47 to 1.05

We examined the effect of the two types of relative risk on the whole population by calculating population attributable risk (PAR).¹³ This is the maximum proportion of the outcome in the total population (exposed and unexposed cases) that is attributable to the exposure. In this study, two PARS (with 95% confidence intervals) were calculated. Firstly, where the outcome is substance misuse and the exposed cases are those exposed to psychiatric illness and secondly where the outcome is psychiatric illness and the exposed cases are those exposed to substance misuse.

RESULTS

Table 1 shows that patients exposed to substance misuse were 1.54 times (95% CI 1.48 to 1.62) more likely to develop psychiatric illness than those not exposed to substance misuse. Patients exposed to psychiatric illness were 2.09 (95% CI 1.99 to 2.02) times more likely to develop substance misuse than those not exposed to psychiatric illness.

Figure 1 shows that the proportion of substance misuse diagnoses occurring before psychiatric diagnoses remained stable over the study period ($t = 0.47$, $df = 4$, $p = 0.65$).

Table 2 shows the proportion of illness in the population potentially explained by exposure to substance misuse or psychiatric illness.

DISCUSSION

Study strengths and limitations

These are the first longitudinal data from the UK relating substance misuse to psychiatric illness in the general population. Exposure and outcome assessment were by a clinician and therefore possibly less vulnerable to the bias that may influence uncorroborated self report. The measures reflected clinically significant substance misuse and psychiatric illness.

The data reported here are comparatively recent and arguably have more relevance to current practice than previous historical studies. However, as the study is based on diagnoses recorded by GPs, there are limitations. They depend on people's use of primary care services and the diagnostic behaviour of GPs and many factors are likely to influence these variables. In most instances, GPs did not record specific substance of misuse and therefore these data cannot be used to clarify causal hypotheses regarding specific drug exposures and specific psychiatric outcomes (or vice versa). In particular these data cannot directly inform the ongoing debate as to whether cannabis use causes psychosis.

Our substance exposure measure was substance misuse perceived to be clinically significant by a GP. In our study the rate of substance abuse over the study period was (0.37%). We are aware of only one study that provides comparable epidemiological data on problematic drug use. In that study, seven estimates were provided, ranging from 0.35% to 0.57%.¹⁴ Substance use not associated with the experience of overt problems is unlikely to have been captured in the current study. Finally, various factors (particularly

aspects of early life adversity) may confound the association between substance misuse and psychiatric illness. We had no data on these factors and therefore no opportunity to consider their influence in our analyses. Caution is therefore required with regard to any causal inference drawn from these data.

Interpretation of study findings

We have already reported that comorbidity of substance misuse and psychiatric illness increased by 62% during the study period.¹ In this study, a diagnosis of substance misuse was associated with an increased risk of a subsequent diagnosis of psychiatric illness (RR = 1.54). This risk was lower than that for psychiatric cases developing substance misuse compared with non-psychiatric cases (RR = 2.09). If the above association between problematic substance misuse and increased risk of psychiatric illness is causal (and we have discussed problems associated with this assumption above) then, on the basis of these data, elimination of all such substance misuse would reduce the incidence of all psychiatric illness by only 0.2% and schizophrenia/psychoses by 0.1%. These very low rates reflect the combination of the relative risk (1.54) and the low rates of problematic substance misuse in the population (0.37%).

These results, therefore, do not suggest that problematic substance misuse makes an important contribution to the population burden of psychiatric illness. Substance misuse that was unrecorded in GPRD data (for example, cannabis use not declared to a GP) may have had an influence that we were unable to detect. It seems unlikely, however, that this influence would have approached the magnitude of the population attributable risks suggested by some, given that visible problem drug users (for example, people receiving substitute opioid prescriptions) tend to have rates of cannabis use substantially higher than those seen in the general population.¹⁵

Over the study period, the population rates of both psychiatric illness and substance misuse in the UK population have increased.^{16, 17} During the same period our study found that most comorbid cases present with psychiatric illness before they present with substance misuse. Furthermore, there was no significant change in this trend over the study period. These data do not support the hypotheses that increasing comorbidity is largely attributable to increasing substance misuse. Comparisons between the 1993 and 2000 national psychiatric morbidity surveys also provide further ecological evidence against an important causal relation between drug use and psychiatric illness. Between these years, reported illicit drug dependence approximately doubled while the reported prevalence of both neurotic and psychotic disorders remained stable. Even if substance misuse causes increased risk of psychiatric illness our finding suggests that attempts to prevent comorbidity by focusing on detection of substance misuse in primary care may meet with limited success. This is because the diagnosis

of psychiatric illness in primary care is much more common than and generally precedes that of substance misuse.

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CONTRIBUTORS

IC and MF had the original idea for this research, which was developed by IC, MF, DM, and PC; MF and PC designed the study; MF analysed the data, and drafted the manuscript; JM redrafted the manuscript and suggested new analyses; All authors contributed to the writing of the manuscript. MF is guarantor.

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